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# Glutathione and Malondialdehyde levels in the serum of type 2 diabetes mellitus with coronary heart disease

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**ABSTRACT**

Diabetes is the most common metabolic disease of humans that its prevalence is increasing worldwide .The status of antioxidants in the serum is one of the most important indicators for controlling and treatment of diabetes, because it plays an important role in protection against oxygen species and oxidative stress .The purpose of this study is to evaluate the serum levels of Glutathione and Malondialdehyde in type 2 diabetes mellitus with coronary heart disease (T2DM-CHD) and comparing them to their levels in healthy individuals. Due to this reason, 50 cardiovascular patients effected by diabetes were studied over a period of two months, the blood samples of were taken from healthy volunteers after 8 hours of fasting, and after centrifugation and separation of serum, biochemical investigations conducted on the samples. The level of malondialdehyde serum in T2DM-CHD group was 19.32 ±16.83 µM/mg-pr and and it increased significantly comparing with healthy group (6/93±3/33 µM/mg-pr). The serum level of glutathione in diabetic group was 15/31±6/58 µM/mg-pr and it decreased significantly comparing with healthy group (34.84±10/06 µM/mg-pr). The evaluation of malondialdehyde and reduction of glutathione in T2DM-CHD decrease may play an important role in the developments of complications in these patients, therefore the using of antioxidant as drug or supplement can probably decrease complications in T2DM-CHD.

**KEY WORDS:** Coronary Heart Disease, Diabetes, Malondialdehyde, Glutathione.

## 1. INTRODUCTION

The growing development of the human societies, changes in the dietary habits and lack of exercise and physical activity, and consequently unwanted adverse effects, such as obesity have caused the development of some risk factors that increase the probability of getting diabetes. Studies have shown that over 21 million people in America, i.e. 10 percent of the country's population, are suffering from diabetes (Dominguez, 2015; Ben Brahim, 2015; Song do, 2015; MacRae, 2015). This non-contagious epidemic disease is growing rapidly worldwide, in such a way, that it is estimated 48 million people would be affected by 2050 (Lee, 2015). Diabetes is the most common metabolic disease in humans leading to consequences such as increase in free radicals and oxidative stress in the body of the patient causing a group of metabolic complications and disorders including reduced insulin secretion or resistance to its function (Kayama, 2015). Recent researches have shown that the tension markers of oxidative stress increase in diabetes (Kayama, 2015). On the other hand many researchers have reported that oxidative stress and free radical oxygen species plays a significant role in the development of diabetic nephropathy and insulin resistance, so that free radicals can greatly trigger other mechanisms in the pathogenesis of diabetes (Kayama, 2015; Ahmadvand, 2012). Also the increase of insulin resistance in diabetes leads to the reduction of the power of antioxidant enzymes, therefore, due to an increase in the markers of oxidative stress in diabetes, the use of antioxidants is beneficial in the treatment, controlling and reducing the signs and symptoms of diabetes (Ahmadvand, 2012; 2013; 2014). Increased production of free radicals or reduction of the levels of antioxidants in diabetes may cause to damage the cell membrane and if this trend continues, malondialdehyde is produced which ultimately leads to the cell death associated with widespread symptoms of the disease (Ahmadvand, 2013; 2014). Malondialdehyde (MDA) is a product of a small but stable lipid peroxidation of unsaturated fatty acids (Ahmadvand, 2012; 2013; 2014). Unstable compounds of free radicals affects lipids, DNA, protein and cells' carbohydrates, but among them, the highest sensitivity is attributed to free radicals production or the decrease of antioxidant levels causing damage to cellular fatty acids oxidation poly saturated fat found in the cell membrane and is known as lipid peroxidation and if this oxidative damage begins, it continues in chain like manner leading to the production of malondialdehyde (Ahmadvand, 2012; 2013; 2014). This situation may ultimately cause cell death associated with wide spread symptoms of the disease (Tangvarasittichai, 2015). Imbalance between the antioxidant defenses and increased production of free radicals can cause a condition known as "oxidative stress" (Tangvarasittichai, 2015). Oxidative stress as result of increased production of reactive oxidants such as oxygen caused by this condition may bring about cellular damage contributing to the development of some diseases (Tangvarasittichai, 2015; Nowotny, 2015).

Glutathione is a specific substrate of glutathione peroxidase and its important tasks are detoxification, antioxidant function and electrophilic conjugation, since glutathione is the most abundant non protein sulfate compound and one of the most important nucleus like of cells, it can play an important role in the detoxification of

external compounds (Diaz-Vivancos, 2015; Aoyama, 2015; Hernandez, 2015). The reaction of xenobiotics with glutathione, increases the solubility of the processes in the cell which is able to be converted to multiprotic acid which is disposed through urine, feces etc. (Cummins, 2011). In this study, the levels of glutathione and malondialdehyde levels in type 2 diabetes mellitus with coronary heart disease (T2DM-CHD) are studied.

## 2. MATERIALS AND METHODS

This study was performed in laboratory of Khorramabad Heart Hospital in December, 2013 and after two months the serum and blood samples of both type 2 diabetes mellitus with coronary heart disease (T2DM-CHD) and healthy individuals were separately transferred to the Razi Herbal Remedies research center of Khorramabad University of medical sciences. After obtaining informed consent form all patients, the samples were taken from all of these individuals after 8 hours of fasting. The blood samples were taken from theses and after centrifugation and separation of serum, some biochemical studies conducted on these samples.

**Measuring Malondialdehyde Test:** The level of Malondialdehyde was measured in accordance with previous study (Ahmadvand, 2014).

**Measurement of glutathione test:** The level of glutathione was measured in accordance with previous study (Ahmadvand, 2012).

**Statistical analyses:** Data were analyzed using unpaired Student's *t* tests. Statistical analyses were performed using the software package used for statistical analysis version 13 (SPSS) for windows software. A P-value of $< 0.05$ was considered statistically significant.

## 3. RESULTS

The serum level of malondaildehyde in T2DM-CHD increased significantly in T2DM-CHD comparing to control group (P=0.003) (figure 1). The level of Glutathione in T2DM-CHD decreased significantly in T2DM-CHD comparing to control group (P=0.002) (figure.2).

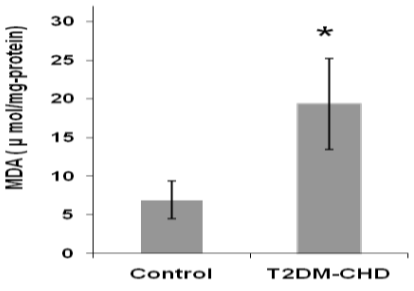


**Figure.1. The level of MDA in type 2 diabetes mellitus with coronary heart disease (T2DM-CHD)**

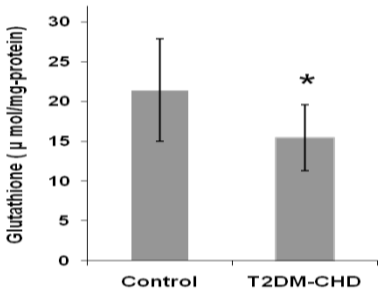


**Figure.2. The level of Glutathione in type 2 diabetes mellitus with coronary heart disease (T2DM-CHD)**

## DISCUSSION

The results of our study showed that the serum level of malondialdehyde significantly increased in T2DM-CHD comparing to control group. The serum level of glutathione significantly decreased in T2DM-CHD comparing to control group.

The study of antioxidant enzymes especially in diabetic patients suffering from cardio vascular complications along with medication and diet changes and also diet therapy can be an effective step in the way of controlling and improving of chronic diseases (Khalatbary, 2016). Researchers reported a significant decreased in antioxidant activities in diabetes type 2 group (comparing to control group) (Ghadge, 2015). Also other researchers found that in type 2 diabetic people, the production of free radicals increases and strengthening of antioxidant drops, as a result the level of oxidative stress increases in these patients (Zalewska, 2015). Recent years researchers began to study oxidative stress and antioxidant enzymes in diabetic patients, since oxidative stress is one of the leading factors in development and progression of diabetes (Palem, 2015). They also studied the verification of Vitamin E supplementation for diabetic patients and oxidative stress (Shirpoor, 2015). Researcher's studies have shown that diabetes is associated with factors like oxidative stress, the increase of free radicals, and decrease antioxidant (Palem, 2015). Much research is currently being done over separation and application of different antioxidants for controlling and inhibition of cardio vascular complication, serum and tissue diabetes (Radomska-Lesniewska, 2015; Nasri, 2015; Abdali, 2015). Today there is a much notice toward these kinds of researches over antioxidants with natural origins so we may achieve new dimensions of these mechanisms and treatment of diabetes (Abdali, 2015). What are important about capabilities of antioxidants are their capability of penetration to biologic membranes and also their speed of action in inhibition and neutralizing of free radicals in the shortest possible time. Hyperglycemia causes non enzymatic glycosylation of enzymes and proteins which are involved in removing of free radicals and lipid metabolisms causing free radicals to increase Due to presence of oxidative stress in diabetic patients and more

production of free radicals, and on the other hand the increase in lipids levels (Pimson, 2014; Tupe, 2014). The need for antioxidants is necessary. There are many different mechanisms reported for oxidative stress in diabetes, among them, "sugar oxidation" is one of the most important ones. Compounds with structure of alpha – hydroxyl aldehydes such as glucose can be converted into enolic form, with revival of transition elements and oxygen they can lead to the production of free radicals (Montero, 2014). The first radical to be created is superoxide which produces $H_2O_2$ by superoxide dismutase, and this active factor in presence of transition element can produce hydroxyl radical that is extremely dangerous and aggressive. When blood glucose is high with binding of sugars to proteins some compounds would be produced which are associated with the production of free radicals (Lincoln, 2013). In addition to above cases, decrease in the glutathione level occurs as a result of disorder in NADPH production level followed by activation of polyol (Piarulli, 2013; Takizawa, 2008). Oxidative stress and free radicals are two effective factors contributing to diabetic disorders, so the control of these factors has an important role in diabetes management, also, based on studies deceased antioxidant activity would increase the probability of oxidative stress in diabetic patients (Takizawa, 2008).

Studies conducted on healthy cases show that antioxidant enzymes are one of the defensive factors against tissue damage caused by oxidative stress, but these enzymes are impaired in diabetic individuals (Ghadge, 2015). Researchers showed that the reduction of glutathione by 20 or 30 percent would lower the cell resistance against toxins and carcinogens and change in the mechanism of xenobiotics increasing the toxicity of metabolites, and consequently leads to cell's damage and death (Diaz-Vivancos, 2015). On the other hand, it is obvious that the increase in glutathione level reduces the carcinogen's cell damage (Singh, 2012). Many scientists believe that "oxidative stress" plays a key role in the pathogenesis of diabetic complications; on the other hand several studies indicate that using antioxidant in diabetic patients can reduce the problems and complications of diabetes & (Ghadge, 2015). The obtained from precious studies have shown that the use of medicine and non- medicine supplements can inhibit free radicals such as vitamin E, vitamin C, Zinc and coenzyme Q10 or natural and organic antioxidants such as Satureja Khozestanica essential oil in diabetic patient plays an important role in strengthening antioxidant defense system and also can be very effective in improving the life of diabetic patients (Ahmadvand, 2012; Ahmadvand, 2012; Tavafi, 2011; Mahmoodi, 2014). In healthy individuals, the antioxidant enzymes protect the cells against damages of oxidative stress, because some antioxidant properties are like vitamins .In diabetic people the balance between production of reactive oxygen and antioxidant levels is interrupted (Ghadge, 2015). Many studies which have been done so far confirm this matter that the presence of oxidative stress in diabetic patients and increase production of free radicals is associated with decreased antioxidant defensive enzymes (Palem, 2015).

Indeed, decreased antioxidants in the body of diabetes type 2 patients are a sign of presence of oxidative stress. Therefore, the individuals having hereditary problems in glutathione metabolism and deceased inner cell glutathione level are more susceptible to oxidative stress, lipid peroxidation and chronic hemolytic anemia.

## 4. CONCLUSION

The presence of meaningful difference in increasing malondialdehyde and decreasing in the glutathione in diabetic patients may play an important role in the development of dangerous disorders of these patients. Since the increasing of malondialdehyde and reduced antioxidant defense mechanism in the body can cause the destruction of the cell, so for this reason, diabetic patients may require more antioxidants. Therefore the using of some antioxidants which are known as "polyphenols" have ant diabetic effects, and can reduce the blood glucose, so finding the herbal remedies being rich in natural antioxidants are beneficial in general health and prevention or treatment of diabetes.

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**Conflict of interest statement:** The authors declare that there are no conflicts of interest.

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